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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,529	10/24/2003	Wei Liu	WYE-010	1341
54623	7590	03/09/2006	EXAMINER	
KIRKPATRICK & LOCKHART NICHOLSON GRAHAM LLP/WYETH 75 STATE STREET BOSTON, MA 02109-1808			RAGHU, GANAPATHIRAM	
			ART UNIT	PAPER NUMBER
			1652	
DATE MAILED: 03/09/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,529	LIU ET AL.	
	Examiner	Art Unit	
	Ganapathirama Raghu	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 October 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 1-7 and 12-23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 October 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>01/26/04, 05/02/05</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-23 are pending in this application for examination. Claims 8-11 are now under consideration. Claims 1-7 and 12-23 remain withdrawn as they are drawn to non-elected invention.

Election/Restrictions

Applicant's election of Group II, claims 8-11 and SEQ ID NO: 2 for prosecution in the reply filed on Jan. 10, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on Jan. 26, 2004 and May 02, 2005 and as the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, Examiner is considering the information disclosure statement.

Drawings

The drawings submitted on 09/15/2003 along with the Application NO: 10/691529 are accepted for examination purposes only.

Specification: Objection

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences within the claims and /or specification. It is particularly noted that Fig.: 1 are sequences, but applicant fails to provide the SEQ ID NO: to these sequences either in the figures or in the figure description of the specification. See particularly 37 CFR 1.821(d).

Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 8 is directed to an isolated polypeptide comprising a fragment of SEQ ID NO: 2, wherein the said fragment comprises at least 200 consecutive amino acids of SEQ ID NO: 2. It is not clear what enzymic activity the said polypeptide is endowed with. Clarification is required.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 is rejected for the phrase "... fragment includes...". The metes and bounds are not clear, Examiner suggests amending the claim to "... fragment comprises...".

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Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 11 is rejected for the phrase "... at least 90% sequence identity". It is not clear to what the 90% sequence identity is referring to in the claim, is the 90% sequence identity to said variant and the fragment as compared to each other or the variant and fragment as compared to SEQ ID NO: 2. Clarification is required.

Claim Rejections 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8-11 are directed to an isolated polypeptide comprising a fragment or variant of SEQ ID NO: 2, wherein the said fragment includes at least 200 consecutive amino acid residues of SEQ ID NO: 2 and wherein the variant and the said fragment have at least 90% sequence identity. Claims 8-11 are rejected under this section 35 U.S.C. 112 because the claims are directed to a "genus" of polypeptides without any associated function. No description of identifying characteristics or functional characterization recognizing all of the sequences i.e., isolated polypeptide comprising a variant of a fragment of SEQ ID NO: 2, wherein the said

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fragment includes at least 200 consecutive amino acid residues of SEQ ID NO: 2 and wherein the variant and the said fragment have at least 90% sequence identity has been provided in the specification for the claims. The specification discloses the isolation of only a single polypeptide with the entire sequence of SEQ ID NO: 2 as having the calcineurin-like phosphoesterase activity encoded by the polynucleotide with SEQ ID NO: 1. No information, beyond the characterization of the polypeptide with SEQ ID NO: 2 having the calcineurin-like phosphoesterase activity have been provided by the applicants, which would indicate that they had possession of the claimed genus of the polypeptides. The specification does not contain any disclosure of the function of all the polypeptides within the scope of the claimed genus. The disclosed information is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus of polypeptides. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide with SEQ ID NO: 2 having calcineurin-like

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phosphoesterase activity, does not reasonably provide enablement for polypeptide comprising a variant of a fragment of SEQ ID NO: 2 or variant of a fragment of SEQ ID NO: 2, wherein the said fragment includes at least 200 consecutive amino acid residues of SEQ ID NO: 2 and wherein the variant and the said fragment have at least 90% sequence identity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 8-11 are so broad as to encompass any polypeptide comprising a fragment of SEQ ID NO: 2 or a variant of a fragment of SEQ ID NO: 2, wherein the said fragment includes at least 200 consecutive amino acid residues of SEQ ID NO: 2 and wherein the variant and the said fragment have at least 90% sequence identity. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are

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conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to amino acid sequence of only one calcineurin-like phosphoesterase i.e., SEQ ID NO: 2. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching the making and using of SEQ ID NO: 2 as an calcineurin-like phosphoesterase, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polypeptides comprising a fragment of SEQ ID NO: 2 or a variant of a fragment of SEQ ID NO: 2, wherein the said fragment includes at least 200 consecutive amino acid residues of SEQ ID NO: 2 and wherein the variant and the said fragment have at least 90% sequence identity, because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the activity of calcineurin-like phosphoesterase; (B) the general tolerance of the calcineurin-like phosphoesterase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue in the polypeptide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with an enormous number of modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

None of the claims are allowed.


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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached on 8 am - 5 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ganapathirama Raghu, Ph.D.
Patent Examiner
Art Unit 1652

Feb. 10, 2006.



MANJUNATH H. RAO, PH.D.
PRIMARY EXAMINER